NINDS Clinical Trials Methodology Course 2025 Syllabus and Course Manual

Introduction

Welcome to the 2025 Clinical Trials Methodology Course (CTMC)! We look forward to working with you over the next several months on your proposed clinical trial. The executive committee found your proposal's premise to be scientifically strong and tackling an important problem in the field of clinical neuroscience.

The goal of the CTMC is to train investigators with limited clinical research experience in the best practices of clinical trial design and execution. Over the next several months, you will participate in small group mentorship meetings, webinars, and a 3-day, in-person conference. The training will deepen your understanding of clinical trials and provide you with the tools to hone your proposed project. We hope that you leave the course with a refined, feasible version of your clinical trial protocol. Ultimately, we aim to increase your likelihood of subsequent extramural funding and a lasting career in clinical research.

The CTMC is divided into 3 phases:

- **Spring –** distance learning and mentorship via small group meetings, webinars, and assignments. During this phase, the clinical trial protocol and logistics are the primary focus. You will be guided to clearly define your experimental intervention, general background, and objectives for your study. This allows you to create a protocol which accurately describes a reproducible clinical research study that is rigorous and feasible.
- **Residential meeting – June 23-26** – intensive, 3-day meeting to workshop the protocol and to network with other trainees & faculty
- **Late summer** – follow up webinars and small group meetings; attention shifts to converting protocol into a research proposal (grant) which effectively provides the scientific justification and summarizes the approach to the study. Incorporating well-defined details into the protocol will make proposal development a much smoother process and make implementing the project, if funded, considerably easier.

The course faculty will invest time in your project; therefore, your participation in ALL aspects of the course, including the residential course, is required to ensure your success.

The CTMC is supported by the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health (NIH) under award number R25NS138633. It is administered by the University of Virginia and Indiana University. Additional support is provided by the American Academy of Neurology. The contents of the course do not necessarily represent the official views of the participating institutions and/or the NIH.

Ethics

All faculty and trainees will consider the projects as confidential and the intellectual property of the developer. Similar to peer review of a grant or paper, the use of any material or idea presented by the trainees is prohibited without written permission. Please report any concerns to the course leadership. Misconduct may be reported to the involved institution(s) and/or the Office of Inspector General, Department of Health and Human Services.

Publications

Please remember to acknowledge the support of NINDS in publications or clinical trials developed from your work in the course. Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as, *"Research reported in this publication was supported by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health under Award Number R25NS138633. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health."*

Table of Contents

Resources

Course Website

https://www.ninds-ctmc.org

Previous Webinars

Recordings of webinars and sessions from prior years are available on our YouTube channel: www.youtube.com/@ninds-ctmc

Recommended Text

Selected chapters from *Clinical Trials in Neurology: Design, Conduct, Analysis (Ravina et al, 2012)* are available in Box (link). Readings will be assigned throughout the small group sessions. The full text may be available from your institution's library; some participants may elect to purchase the full text.

Example Grant Materials

Links to multiple grant-related resources are provided throughout the syllabus.

NIH & NINDS Resources

The NINDS provides a Clinical Research Toolkit on their website.

The NIH developed a "Phase 2 and 3 Clinical Trial" protocol template that is the standard template used for this course. A word version of this protocol template can be found in your individual Box folder and online (see: Word Version of Final Template).

Electronic Platforms

Zoom

The course will use Zoom as the primary cloud-based meeting platform for small group meetings, webinars, office hours, and other virtual activities. We encourage each participant and faculty member to use a webcam to allow their video to be 'on' during Zoom meetings. Appointments with Zoom links/meeting information will be added to your email calendar. It is preferable to use a computer and webcam, but you can also use phone or tablet apps as necessary. If you must use a telephone, call in information can be found in appointments. Do not use a telephone AND computer audio (this causes feedback).

- UVA Zoom FAQs: https://in.virginia.edu/zoomfaqs
- Zoom Support Center: https://support.zoom.com/hc/en

Box

UVA Box (https://virginia.account.box.com/login) will be the document sharing platform for the course. Links will be provided to any readings assigned during the course. You will each have a subfolder (labeled with your last name) within your small group folder, and you will be expected to upload all your documents in it. Faculty members will provide feedback directly within the documents (assuming that they are submitted with enough lead time prior to the respective meeting). Documents should be provided in Word format (.doc or .docx) to allow faculty to comment directly within the document. Meeting recordings will also be stored in Box. Please check your junk mail folder if you have not received an invitation.

- **Login steps for external users**
  - Select 'Not a part of the University of Virginia' option on the right side
  - If you have an existing Box account, use your email address & password to sign in. If you do not have an existing Box account, select 'Sign Up' in the upper right-hand corner. Individual plans can be created for free.
  - Once you log in, folders that have been shared with you will appear in the navigation.

- How to use UVA Box: https://in.virginia.edu/box-use
- Box Support Center: https://support.box.com/hc/en-us

Evaluation Surveys

We will send various surveys via Qualtrics and REDCap throughout the duration of the course and beyond. Survey responses are used to evaluate the effectiveness of the course overall, as well as specific programming. The responses shared in the surveys will be treated confidentially whenever possible and will not impact your participation in the course.

Surveys will include:

- Small group evaluations
- Webinar evaluations
- Residential Course evaluations (link to be provided at the meeting)
- Outcome Assessments
    - The outcomes survey aims to track what has happened to you, your research overall, and your CTMC project after the course. The outcomes surveys will be sent annually via email after you complete the course. These surveys are **vitally important** as they allow us to assess the course's impact and justify continued funding. We thank you in advance for your future responses.

After the course

We hope that you form a long-lasting network of colleagues and mentors during your time in the course.

You will continue to receive annual outcomes surveys after you complete the course (see above), as well as updates related to future calls-for-applicants, course milestones, and other important announcements. We rely on our alumni to spread the word about the program, and to refer prospective participants to us.

There are several opportunities to continue your engagement with the course:

Mock study sections

The executive committee offers previous trainees the opportunity to submit their proposals for mock study section review. These sessions typically take place in the fall. Details about how to apply and participant will be sent via email.

Reunion at the American Academy of Neurology (AAN) Annual Meeting

Trainees from the current and previous cohorts are invited to join the annual AAN-sponsored NINDS CTMC Meeting and Reunion which is held each spring at the AAN Annual Meeting.

Alumni are asked to provide updates related to their project and their clinical research careers. The reception provides an opportunity to hear about impactful research from CTMC alumni, and to network with faculty and NINDS representatives. You will receive invitations via email.

Course Outline

1. Baseline Tasks:

- ❑ Review 2025 Syllabus and Course Manual
- ❑ Attend first webinar, Course Orientation & Trainee Elevator Pitches, on **March 21st from 12-1pm ET**
    - o Please prepare a 3-minute "elevator pitch" to introduce yourself and your project to the faculty and other trainees.
    - o If you cannot attend in person, please provide a 3-minute recorded "elevator pitch" to be played during the meeting. The meeting recording will be provided to you.
- ❑ Review instructions for Box (page 3) and confirm that you can log in and access the assigned folders.
- ❑ Confirm that you have events on your calendar for (1) recurring small group meetings, (2) webinar series, (3) office hours (optional), and (4) residential meeting in June.
    - o *Contact Megan Wardius if you have trouble with Box or if you are missing calendar events.*
- ❑ Read and review the NINDS Transparency in Reporting Guideline: Improving the Quality of NINDS-Supported Preclinical and Clinical Research through Rigorous Study Design and Transparent Reporting
- ❑ Complete the Session 1 assignments prior to your first small group meeting. The first small group meetings will occur the week of March 31st or April 7th, depending on your group's availability.

2. Webinar Series:

Webinar Logistics:

- o Unless otherwise specified, webinars will be held every other **Friday from 12:00 – 1:00pm ET**.
    - o *Please contact Megan Wardius if you do not have the webinar calendar invitations.*
- o Real-time attendance and participation in the webinar series is recommended whenever possible.
- o Recordings will be posted to the course YouTube channel for those who cannot attend in real time.
- o Please EVALUATE each webinar afterwards as we use the feedback to improve them and incorporate helpful suggestions: 2025 Webinars Evaluation Survey

2025 Webinar Schedule: Fridays 12-1pm Eastern Time

March 21:	**Orientation & Elevator Pitches** *Please prepare a 3-minute "elevator pitch" to introduce yourself & your project to the faculty and trainees.*
April 4:	**Comparing Clinical Trial Protocols to Grant Applications** – Presented by Roger Lewis, MD, PhD
April 25:	**Avoiding Pitfalls in Early Phase Clinical Trials** – Presented by Chris Coffey, PhD; Will Meurer, MD
May 2:	**Surviving Peer-review of Clinical Trial Manuscripts** – Presented by Roger Lewis, MD, PhD
May 16:	**Outcome Measures** – Presented by Harold Adams, MD

May 30:	**Incorporating Participants' Perspectives in Clinical Trial Design** – Presented by Sophia Wang, MD
June 6, 2pm ET:	**Introduction to NINDS Networks** – Presented by Chris Coffey, PhD; Valerie Durkalski-Mauldin, PhD; and Pooja Khatri, MD, MSc **Please note the change in time (2pm ET) for this session!*
June 13:	**What to Know About Sample Size** – Presented by Sharon Yeatts, PhD
July 11:	**Specific Aims** – Presented by Jordan Elm, PhD, and Robert Silbergleit, MD
July 25:	**Data Science in Clinical Trials** – Presented by Paul Perrin, PhD; Thomas Stewart, PhD; and John Van Horn, PhD

Previous Webinar Recordings:

Recordings from previous CTMC webinars can be accessed via our YouTube channel.

3. Office Hours

Office hours are open times where executive committee members and core faculty are available to answer questions related to protocol development, webinar topics, or other general topics. Attendance is only required when you have a specific question(s) to discuss.

Office hours will be held weekly on **Tuesdays from 11:30 – 12:00 ET**.

Please sign up in advance using this sheet**.** This will allow us to maximize efficiency and ensure that the appropriate faculty are available to answer your questions.

Meeting information will be added to your calendar, and is provided here:

Meeting URL:
https://virginia.zoom.us/j/99245989272?pwd=Qnh5a8bcRYT4my750c1ryXPyLCZgym.1&from=addon
Meeting ID: 992 4598 9272
Passcode: 224271

4. Small Group Sessions

The goal of the small group sessions is development of a protocol synopsis, and a draft protocol, through mentorship from dedicated core faculty. Each small group includes two clinical faculty and one biostatistical faculty member who will use their unique expertise to collaboratively guide you through protocol development.

All sessions will be **60 minutes** long and will be conducted via Zoom; event invitations will be sent to your calendar. Course participants are expected to attend every session.

Meetings will be set up to be recorded and saved in the group's private Box folder; this for note-taking and internal review purposes. Please contact Megan Wardius to change the auto-record settings if you do not wish to be recorded.

Note taking is highly encouraged; historically, it has worked well to assign a note taker for each session.

Schedule

March 31 – June 23	
Pre-residential course sessions – 1st session will take place the week of March 31 or April 7	12 weeks / 9 sessions **Scheduled per each group's availability*
Residential Meeting: June 23-26	

June 30 – Aug 1	
Post-residential course sessions	5 weeks / 3 sessions **Scheduled per each group's availability*
July 11th:	**'Final' protocol synopsis due**

Expectations for weekly assignments:

- **Assignments are due as soon as possible, and no later than 48 hours prior to the week's session.** Assignments submitted less than 48 hours in advance may not allow sufficient time for faculty input. For groups that meet on Monday, please submit your assignments on Friday rather than over the weekend.
- Each trainee will have one master document that is uploaded to Box. This document will contain the protocol synopsis and full protocol draft, including statistical analysis plan. **All changes should occur in the master document on an ongoing basis.** Revisions to previously completed sections are encouraged as your discussions & knowledge delve deeper.
- Each trainee will have a checklist and audit summary document that is privately shared with the group faculty. **Trainees will keep the checklist up to date by noting progress and briefly describing the major changes that have occurred each week.** This will allow faculty to effectively track how the protocol has evolved over time and help to avoid repetitive or conflicting feedback.
- Faculty will directly comment within the protocol document to ask questions and offer feedback. Faculty are expected to review the latest document prior to the week's session.
- The NINDS protocol template is the standard template to be used in the course; trainees who wish to use an alternative template must discuss with their group's faculty for approval during one of the early small group sessions.

Outline of Sessions

Individual groups may deviate from this outline based on specific needs and interim progress; group faculty will provide additional guidance regarding weekly assignments.

4.1 Session 1: Introduction & Defining Clinical Question

❑ **Scheduling:**
- An availability spreadsheet will be provided prior to the first small group meeting to facilitate a conversation with the group about which weeks you will be holding sessions.
- Course participants are expected to attend all small group sessions for the year; if multiple faculty members are unavailable for a given week, it should likely be cancelled.
- You can contact Megan Wardius (mew5j@uvahealth.org) to edit or remove any dates on the calendar.

❑ **Assignment:**
- Prepare a 5-minute oral presentation of your project idea to be given during the first session (no slides).
  - Focus on your clinical trial and its significance. Highlight high yield topics such as disease, phenotype, preclinical justification and the rigor of such research/data, and the scientific premise of your trial.
- Protocol synopsis: Title, Study Description, & Study Population
- Protocol: Prepare a 1-3 page "Study Rationale & Background" section for a protocol describing why your clinical trial idea is significant. Confirm what protocol template you will be using (most will use the NINDS template).
  - The overall goal is to let the reader understand why your project is significant. For example:
    - Does your project address an unmet need?

- Is the study question that you are asking novel?
- Does your study question address an important disorder/disease/problem?
- Why is it relevant to the clinical environment?
- Include references.

4.2 Session 2: Outcome Measures: Study Objectives & Endpoints

❑ **Reading:**
- Review Chapter 7 in Ravina: Chapter 7: Selecting Outcome Measures

❑ **Assignment:**
- Protocol synopsis: Objectives & Endpoints (including primary, secondary & other objectives/endpoints)
- Protocol: Begin the objectives and endpoints section of the full protocol.

4.3 Session 3: Overall Trial Concept: Design Selection & Initial Feasibility

❑ **Readings:**
- Review Chapters 2 and 4 in Ravina (course text)
  - Chapter 2: The Sequence of Clinical Development
  - Chapter 4: Fundamental of Biostatistics

❑ **Assignment:**
- Protocol synopsis: Study Duration, Participant Duration; revisit Study Description
- Protocol: Draft a schema of your study to illustrate your study design (e.g., study arms, key timepoints and study procedures). Begin the study design and statistical analysis sections, **including sample size**, of the full protocol.

4.4 Session 4: Study Population

❑ **Reading:**
- Review Chapter 27 in Ravina (course text): Chapter 27: Clinical Trial Planning - An Academic and Industry Perspective

❑ **Assignment:**
- Protocol synopsis: Revisit study population
- Protocol: Draft the inclusion and exclusion criteria for your participants. Begin the study population section of the full protocol.
- Other: Consider the feasibility of recruitment and retention in your specific population and how community consultation could inform your trial design. Research the demographics of your study population and how that will influence your enrollment targets & recruitment strategies.

4.5 Session 5: Treatment Allocation & Interventions

❑ **Assignment:**
- Protocol synopsis: Revise as needed (study description, description of intervention, etc.)
- Protocol: Begin the study intervention and discontinuation sections.

4.6 Session 6: Measurements, Endpoints, and Data Management

❑ **Assignment:**
- Protocol synopsis: Revise as needed (objectives, endpoints, etc.).

- Protocol: Begin the study assessments section, considering both safety and efficacy measurements.

4.7 Session 7: Statistical Analysis Strategy – Sample Size Detailed, Primary Analysis, Secondary Endpoints, Exploratory Analyses

❑ **Assignment:**

- Protocol synopsis: Revise as needed.
- Protocol: Revise statistical analysis plan as needed, including sample size calculations.

4.8 Session 8: Adverse Events, Data and Safety Monitoring, and Interim Analyses

❑ **Assignment:**

- Protocol synopsis: Revise as needed.
- Protocol: Revise statistical analysis plan as needed. Consider the adverse events and regulatory sections of the protocol.

4.9 Session 9: Budget

❑ **Readings:**

Readings:

- Review the following article: Developing an Investigator Site Budget for Clinical Trials
- Review the following presentation and look at the schema examples: UNC Chapel Hill 3rd Annual Symposium for Research Administrators: Budgeting for Proposals

❑ **Assignment:**

- Other: Draft a budget and budget justification.
- Protocol synopsis: Revise as needed.
- Protocol: Revise assessments as needed.

RESIDENTIAL COURSE

❑ **Assignment (throughout meeting):** Revise your protocol synopsis and make notes about necessary changes to the full protocol draft. Your "final" protocol synopsis will be due 2 weeks following the end of the residential course.

4.10 Session 10: Full Protocol Draft

❑ **Assignment:** Update sections of your full protocol based on the content of the residential course.

4.11 Session 11: Specific Aims, Research Strategy, Research Plan – Converting a Protocol into a Grant

❑ **Assignment:** Draft a specific aims page

❑ **Grant Example Materials:**

- REACHOUT – an R01 single site trial:
  - R01 Summary statement:
    - REACH OUT R01 Grant Summary Statement
    - The grant was submitted (and subsequently funded in this format)
  - R34 Summary statement:
    - The grant was submitted twice in this format and was not funded either time
    - REACHOUT R34 Grant Summary Statement First Submission
    - REACHOUT R34 Grant Summary Statement Second Submission
- NIH websites:

- The NIH offers user guides and writing resources on their websites, including:
  - Research Plan Drafting Resources: NIH "Write Your Application" page
  - Research Plan Drafting Resources: NIH "Write Your Research Plan" page
  - Research Plan Drafting Resources: NIH "Sample Applications and More" Page
- Features:
  - Provides good overview of how to write scientifically
  - Gives good information on how to write a grant that meets the current NIH requirements
  - Focuses and explains well how to communicate clearly
- Caveats:
  - Almost all of the examples are either preclinical or translational (and therefore not as useful for a strictly clinical focus)
  - The major takeaway from all of these resources is that although the page content and example do not match a clinical trial R01 grant application in a 1:1 sense, the principles that they review, the writing style, and most importantly the structured approach are applicable to any well-written grant application proposal that falls within the purview of the Clinical Trials Methodology Course.

4.12 Session 12: Human Subjects Sections & Wrap Up

❑ **Assignment:** Draft key sections of human subjects plan as requested by your faculty – recruitment & retention, inclusion of individuals across lifespan, inclusion of women and minorities, planned enrollment, study timeline, protection of human subjects, DSMB, structure of study team, dissemination plan.

Small Group Evaluations

Surveys will be distributed via email to provide evaluation of small group activities. The responses will be used to improve the small group meetings for future courses.

Any concerns about small group activities that occur during the course and require prompt attention should be sent via email to the course directors and/or the program manager, Megan Wardius, in real-time.

5. Residential Meeting

The residential meeting is a 3-day, intensive component of the course will take place in-person in Charlottesville, Virginia.

The meeting will be held Monday, June 23 – Thursday, June 26. Travel and accommodations will be provided through the course.

A variety of course lectures, small group meetings, office hours, and other activities will be scheduled during the meeting. A complete agenda will be provided closer to the meeting. Attendance at all sessions is required unless otherwise specified. Readings and/or specific assignments may be set by course faculty.

General schedule:

- **Monday, June 23rd –**
  - Morning/afternoon: Travel day for most participants
  - 6:00-8:00pm: Welcome reception

- **Tuesday, June 24th –**
  - 8:00am – 4:45pm – Meeting sessions
  - 6:00-8:00pm – Small group dinners
- **Wednesday, June 25th –**
  - 8:00am – 5:15pm – Meeting sessions
  - 6:30-8:30pm – Group dinner
- **Thursday, June 26th –**
  - 8:00am – 1:00pm – Meeting sessions
  - Afternoon/evening: Travel day for most participants

After the Course

Information about after the course activities can be found on page 3.